UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/502,984	02/11/00	LUO	P A-68126-1/RF

HM12/0131

FLEHR HOHBACH TEST
ALBRIGHT & HERBERT LLP
FOUR EMBARCADERO CENTER SUITE 3400
SAN FRANCISCO CA 94111-4187

EXAMINER	
ZARA, J	
ART UNIT	**PAPER NUMBER**
1635	7

DATE MAILED: 01/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/502,984	Applicant(s) LUO ET AL.	
	Examiner Jane Zara	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sh t with the corr spondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

File

DETAILED ACTION

Claims 1-19 are pending in the instant application.

Oath/Declaration

The declaration is objected to because it does not include all the inventors that are listed.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 recites the limitation "the signaling" in the last line of the claim (line c). There is insufficient antecedent basis for this limitation in the claim.

Claims 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "signaling" (in line c of claim 11) needs to be defined (i.e. Does this refer to the initiation of a signaling cascade, such a kinase cascade, or does this more simply refer to the emission of some signal or marker by the immobilized or bound ligand (fluorescence or radioactivity?).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1-4, 6-9 and 11-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Stahl *et al.*

Stahl *et al* teach methods of screening for ligand analogs which bind to human cytokine cell surface receptors of eukaryotic, prokaryotic or viral cells, comprising determining the binding of naturally occurring ligands and ligand analogs to cell surface receptor analogs, whereby the protein sequences of such receptor analogs are less than 90% identical or homologous to corresponding naturally occurring cell surface receptors, which receptor analogs comprise an extracellular domain, alone or in combination with a transmembrane domain, or additionally contain a cytoplasmic domain, and whereby the receptor analogs bind natural ligands at the same or higher binding affinity than naturally occurring cell surface receptors, and further whereby the non-naturally occurring cell surface receptors optionally comprise a chimeric receptor which contains an extracellular domain and a cytoplasmic domain from at least two different naturally occurring receptors, or comprises an exogenous dimerization domain optionally linked to an internal or extracellular domain, and wherein said cell surface receptor

analog comprises two monomers of naturally occurring receptors which are crosslinked, and which may be heteromeric or homomeric receptors, and which receptor analogs may be in an aqueous solution. Stahl *et al* teach recombinant chimeric cell surface receptor complexes comprising at least two different monomers which differ in amino acid sequences from each of their respective naturally occurring human cell surface receptors, whereby said chimeric receptor binds natural ligands at the same or higher binding affinity than naturally occurring cell surface receptors (See entire document, especially column 3, line 15-column 6, line 12; column 6, line 16-column 12, line 14; claims 1-17).

Claims 1-4, 6-12 and 17-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Jin *et al.*

Jin *et al* teach recombinant chimeric human cell surface receptor complexes, including cytokine receptors, comprising at least two different monomers of naturally cell surface receptor analogs and which bind natural ligands (for original naturally occurring receptors from which receptor analogs are based) with the same or higher binding affinity than non-chimeric, naturally occurring cell surface receptors. Jin *et al* also teach methods of screening for ligand analogs comprising determining the binding a said candidate ligands to non-naturally occurring cell surface receptor analogs which comprise less than 95% amino acid sequence identity or homology with the extracellular domain of a corresponding naturally occurring cell surface receptor, which receptor analog is on the surface of a prokaryotic, eukaryotic or viral cell, or in aqueous solution, and which receptor analog comprises an extracellular domain optionally linked

to a transmembrane domain, and further optionally linked to a cytoplasmic domain, and wherein the receptor analog has a different structure than the corresponding naturally occurring cell surface receptor, which determination of structural differences is based on computer analysis (See entire document, especially figure 2; column 3, line 49-column 6, line 65; column 13, line 37-column 14, line 60; example 5, column 17-column 18; claims 1-7).

Claims 1-4, 6-12, 18 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Ichijo *et al.*

Ichijo *et al* teach methods of screening for human cell surface receptor ligand analogs comprising determining the binding of said ligand analogs to non-naturally occurring cell surface receptor analogs comprising less than 95% amino acid identity or homology, and wherein receptor analog binds to the corresponding natural ligand at same or higher binding affinity than naturally occurring cell surface receptor, and which receptor analog comprises an extracellular domain, optionally linked to a transmembrane domain, and additionally optionally linked to a cytoplasmic domain, whereby the extracellular and cytoplasmic domains are optionally from two different naturally occurring cell surface receptors, and which variations in amino acid sequence and structure have been designed based on computer program calculations (See entire document, especially abstract; column 3, line 40-column 8, line 40; column 9, line 9-column 11, line 48; example 2, columns 12-14; example 6, column 19; claims 1-3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stahl *et al*, Jin *et al* and Ichijo *et al* as applied to claims 1-4 and 6-19 above, and further in view of Ochoa *et al*.

The claims are drawn to methods of screening for ligand analogs which bind to human cytokine cell surface receptors of eukaryotic, prokaryotic or viral cells, comprising determining the binding of naturally occurring ligands and ligand analogs to cell surface receptor analogs, whereby the protein sequences of such receptor analogs are less than 90% identical or homologous to corresponding naturally occurring cell surface receptors, which receptor analogs comprise an extracellular domain, alone or in combination with a transmembrane domain, or additionally contain a cytoplasmic domain, and whereby the receptor analogs bind natural ligands at the same or higher binding affinity than naturally occurring cell surface receptors, and further whereby the non-naturally occurring cell surface receptors optionally comprise a chimeric receptor which contains an extracellular domain and a cytoplasmic domain from at least two different naturally occurring receptors, or comprises an exogenous dimerization domain optionally linked to an internal or extracellular domain, and wherein said cell surface receptor analog comprises two monomers of naturally occurring receptors which are crosslinked, and which may be heteromeric or homomeric receptors, and which receptor analogs may be in an aqueous solution, the binding of which said ligands and ligand analogs occurs on cell surface receptor analogs which are on cellular surfaces, in solution, or attached to a solid support. The claims are further drawn to chimeric cell surface receptor complexes comprising at least two different monomers which differ in amino acid sequences from each of their respective naturally occurring human cell surface receptors, whereby said chimeric receptor binds natural ligands at the same or higher binding affinity than naturally occurring cell surface receptors.

Stahl *et al*, Jin *et al* and Ichijo *et al* are relied upon as cited in the 102 rejections above.

These primary references do not teach the binding of cell surface receptors or analogs thereof to ligands or ligand analogs, comprising cell surface receptors or analogs thereof which are bound to solid supports.

Ochoa *et al* teach the binding of ligands to cytokine cell surface receptors, which receptors are bound to a solid support (column 4, lines 25-30).

It would have been obvious to one of ordinary skill in the art to attach cell surface receptors or analogs thereof to solid supports to measure ligand binding because the attachment of such receptors to solid surfaces and the subsequent binding of ligands to immobilized receptors had been taught previously in the art by others including Ochoa *et al*. One of ordinary skill in the art would have been motivated to attach receptors to solid supports and measure the binding of ligands to them because this method provides for the facile separation of bound ligands from unbound ligands in solution, thereby circumventing a separation step comprising the removal of ligand-receptor complexes from unbound receptors and unbound ligands in a solution. One of ordinary skill in the art would have expected that using immobilized receptors to measure ligand binding provides a means of determining affinity constants for ligand-receptor binding without having to separate bound receptors from unbound receptors in solution. One of ordinary skill in the art would also have expected that the means chosen for attaching such receptors to solid surfaces does not alter the binding affinity of said receptors for said ligands because there are a myriad of ways to attach proteins to solid surfaces, including through

different chemical linkages, and using various linkers, and one of ordinary skill in the art would have expected that a means of attachment would be determined through routine experimentation whereby the receptor's binding activity remains unaltered upon immobilization to a solid support.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to

the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

January 28, 2001

ANDREW WANG
PATENT EXAMINER
TC1600